REMARKS

Claims 1-8 are currently pending in the present application.

Borokov does not disclose "excision"

Borokov does not disclose use of an excisionase to **completely remove** intervening sequences. Borokov retains residual "recombinase sites":

Borokov Product = ~R1-F1-R1-F2-R2-….-FN-RN-R1~

The present invention uses a combination of recombinases and excisionases to assemble the DNA and then remove the vector and recombinase site leaving a series of fragments **without** intervening DNA sequences:

Disclosed Product = ~F1-F2-F3-…-FN~

Borokov does not disclose site specific excision sites "**oriented in an appropriate orientation for excision**" that will "bring the second fragment **adjacent** to the first fragment." Borokov does not anticipate the current claims because Borokov does not disclose each and every element of the claimed invention.

Declaration of Dr. Bennett antedates Cheo

According to MPEP §2136.05, "When a prior U.S. patent, U.S. patent application publication, or international application publication is not a statutory bar, a 35 U.S.C. 102(e) rejection can be overcome by **antedating the filing date** (see MPEP § 2136.03 regarding critical reference date of 35 U.S.C. 102(e) prior art) of the reference by submitting an affidavit or declaration under 37 CFR 1.131."

The Applicant's present invention was conceived and reduced to practice prior to the filing date of US2002007051 by Cheo. The attached Declaration under USC 1.131 by Dr. Bennett describes the recombination system and its use. The attached Exhibits A & B demonstrate the invention was conceived and reduced to practice prior to December 10, 1999. Therefore Cheo is removed as a reference.

Difference between "Excisionase" and "Recombinase"

Applicants respectfully request the examiner reconsider the term "recombinase" versus the term "excisionase." Applicants used the terms within the specification to indicate 2 separate

reactions. A recombinase uses two recombination sites, removes the intermediate DNA, and leaves a single recombination site intact. A recombinase is active in a specific reversible reaction at the recombinase site. Recombinases are used to insert or remove specific DNA leaving the recombinase site intact. Excisionases use two inverted sites, remove the intermediate DNA **and the excisionase specific binding site**, leaving a final DNA product without any intervening sequences. Some recombinases may function as excisionases, but the molecular reaction is different. The DNA template for excision must be inverted and the reaction product leaves no recombination site in the final product. The specification uses "a site specific excision site (e.g. a recombinase site in the reverse orientation to that found in the recipient DNA)" to completely remove intervening DNA sequences (¶10). The specification differentiates the recombinase reaction and the excisionase reaction and does **not** use the terms interchangeably.

"Excisionase" provides a different product

The use of the term "excisionase" is not "definitional" because it describes a separate molecular reaction than recombinases using different starting materials to generate a different product. Because the product of the excisionase is different than the product from a recombinase, the overall reaction scheme and final products are different. In FIG. 2, the products of excision are demonstrated where the intervening sequences between **and including** the *hix* sites are completely removed and the product is fragment A **adjacent** to fragment B. No intervening sequences remain. This is demonstrated again where the intervening sequences between and including the *TnE* sites are completely removed and the final product is AB adjacent to fragment C. Again, no intervening sequences remain.

Claims require "Excisionase"

The claims specifically state that the "site specific excision sites are oriented in an appropriate **orientation for excision** with undesired vector sequences therebetween." The claimed method further requires removal of "the undesired vector sequences and bring **the second fragment adjacent to the first fragment**." The requirement for an excisionase reaction is drafted in the claim. This is unique from Borokov which does not mention or contemplate the use of the excisionase reaction to remove intervening vector sequences bringing the fragments "**adjacent**" to each other. Although Cheo has been antedated and no longer qualifies as art under §102(e) or §103, Cheo uses methods similar to Borokov for modifying recombinase sites

and improving specificity. This specificity is required to prevent recombination with residual recombinase sites. Neither Borokov or Cheo describe the methods of the current invention as claimed because neither completely removes the excisionase site and leaves the desired fragments **adjacent** to each other.

CONCLUSION

The references cited do not disclose an excisionase reaction that removes the vector sequences and excisionase sites leaving the product DNA fragments adjacent to each other. Therefore each and every element of the claimed invention is not disclosed, anticipated or obvious.

In view of the foregoing amendments and remarks, Applicant respectfully submits that the pending claims are in condition for allowance, and favorable action is hereby requested. If a telephone interview would be of assistance in advancing prosecution of the subject application, the Examiner is requested to telephone the undersigned at the number provided below. Applicant believes all fees due have been paid. If, however, a fee is due, the Commissioner is hereby authorized to charge such fee to Deposit Account No. 50-3420, Attorney Docket No. 31175413-003002 (HOUMDB).

Dated: November 17, 2006

Respectfully submitted,

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